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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,406	11/23/2005	Christelle Pragnon	021305-00214	2881

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EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1657	

DATE MAILED: 11/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/539,406	PRAGNON ET AL.	
	Examiner	Art Unit	
	Paul C. Martin	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 23 November 2005 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 06/17/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-12 are pending in this application and were examined on their merits.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 12/19/2002.

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they fail to show any lines or graphs indicating actin polymerization as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." The corrected drawings should not contain any new matter.

If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: The French word "tampon" is used repeatedly in place of "solution" or "buffer".

Appropriate correction is required.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 contains the language, "the total dosage of proteins in the lysate"; it is unclear whether this constitutes a method step or a description. If it is a method step it is unclear what the proteins in the lysate are being dosed with and to what purpose. Claims 6 and 12 further contains the language, "substances necessary for endogenous actin polymerization and protection of the lysate proteins."

It is unclear what these substances are, what they are added to and how much of these unspecified substances are added. Claims 7-11 are rejected as being dependent upon Claim 6.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 contains the use of the word "tampon" which is a French word for a solution or buffer. For purposes of clarity, substitution of buffer or solution in place of tampon is suggested.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 recites the limitation "the said substance" in line 5 of the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 7 further recites the limitation, "in the presence of an appropriate quantity"; it is unclear what amount constitutes an appropriate quantity.

Claims 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-10 are drawn to the application of the method of any one of claims 1 to 6 to the evaluation of the invasive character of the cells, evaluation of the oncogenicity of the cells and prediction of the sensitivity of the cells to an anticancer treatment respectively. It is unclear how these goals will be accomplished, as there are no further method steps or description for making these determinations. Claim 11 is rejected as being dependent upon rejected Claim 10.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Tellam *et al.* (1986).

Tellam *et al.* teaches a method to determine the nucleating activity in tumorigenic cells wherein tumorigenic cells are lysed in non-denaturing conditions and centrifuged to remove cellular debris, fluorochrome labeled actin monomers are added to the lysate along with substances necessary for the polymerization of endogenous actin and protection of the lysate proteins, measuring the quantity of polymerized actin in the steady state of the lysate, and comparing the quantity of polymerized actin monomers incorporated into the actin filaments from the cell lysate of tumorigenic cells to the reference quantity of polymerized actin from non-tumorigenic cells Pg. 1285, Lines 8-28 and 33-39 and Pg. 1286, Lines 1-13 and Fig. 1).

Tellam *et al.* teaches a cell re-suspension medium, substances necessary for the endogenous actin polymerization and protection of the lysate proteins, solutions of actin monomers labeled with a fluorochrome, the extracts of tumorigenic and non-tumorigenic cells and reaction buffers (Pg. 1285, Lines 8-28 and Pg. 1286, Fig. 1 legend).

Claims 1-3, 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Malicka-Blaszkiewicz *et al.* (1995).

Malicka-Blaszkiewicz *et al.* teaches a method wherein the quantity of polymerized F-actin in cancerous and control cell lysate in the steady state are compared, wherein the cells are lysed in non-denaturing conditions, centrifuged to remove cellular debris, suspended in a buffer necessary for endogenous actin polymerization and the protection of lysate proteins, and the quantity of polymerized actin in the steady state of the lysate between the cancerous and control cells is compared (Pg. 115, Column 2, Lines 30-35 and Pg. 116, Column 2, Lines 1-37 and Pg. 117, Fig. 1).

Malicka-Blaszkiewicz *et al.* teaches that a high level of actin polymerization is a prerequisite for the formation of pseudopodia, which in turn are necessary for the infiltration of cells into tissues (invasion) and eventually for efficient metastasis formation (oncogenicity) (Pg. 118, Column 1, Lines 1-8).

Malicka-Blaszkiewicz *et al.* teaches that actin is a possible marker in the evaluation of the stage of tumor growth and its metastatic potential, and could be expected to pave the way for therapeutic intervention, aimed at stopping and possibly reversing the process of metastatic growth with the use of drugs affecting actin polymerization (Pg. 118, Column 1, Lines 22-31).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tellam *et al.* (1986) in view of Menu *et al.* (2002).

The teachings of Tellam *et al.* were discussed above.

Tellam *et al.* did not teach a method wherein the quantity of polymerized actin corresponds to the sum of all of the F-form actin, wherein the measurement of the quantity of actin in the steady state is carried out by static fluorescence polarization in the presence of actin monomers bound to a fluorochrome which are added to the cellular lysate in a proportion ranging from $1/80^{th}$ and $1/1600^{th}$ in relation to the quantity of endogenous actin, the monomers being incorporated into actin filaments (f-actin) formed during endogenous actin polymerization of the lysate, wherein the method is used to evaluate the invasive character of the cells, or a kit including a cell re-suspension medium for the cell lyses, substances necessary for the endogenous actin polymerization and the protection of the lysate proteins,

a solution of actin monomers bound to a fluorochrome, an actin polymerization solution, a general actin solution, and optionally the extracts of aggressive and non-aggressive reference cells.

Menu *et al.* teaches a method of determining the tumor aggressivity of cancerous cells by measuring the quantity of polymerized f-actin in the steady state of lysate of the cells and comparing the value of the quantity of polymerized f-actin in the cancerous cells to a reference value of non-migrating cells (Pg. 131, Lines 1-12 and Fig. 4) and exposing the cells to the actin polymerization inhibitor latrunculin-A and determining the capacity of the latrunculin-A to restore the quantity of polymerized actin in the steady state to that of the non-migrating cells (Pg. 131, Fig. 4) and wherein the invasive character of the treated vs. non-treated cells is determined (Pg. 132, Fig. 6).

Menu *et al.* teaches that F-actin becomes polarized when the cells are migrating, in contrast to non-migrating cells and that this polarization can be visualized by fluorescence and confocal laser scanning microscopy and quantified by fluorometry and flow cytometry (Pg. 124, Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method to determine the nucleating activity in tumorigenic cells as taught by Tellam *et al.* above with the method of quantifying polymerized F-actin as taught by Menu *et al.* because both methods are drawn to the detection and quantification of actin polymerization in cancer cells. One of ordinary skill in the art would have recognized that the use of fluorescently labeled monomers added to a cellular lysate, and incorporated into f-actin filaments during endogenous actin polymerization as taught by Tellam *et al.* could have been measured by the fluorescence polarization method of Menu *et al.* and one of ordinary skill in the art would have been motivated to combine these two methods because of the advantage described by Menu *et al.* wherein aggressive migrating (invasive) cancer cells can be visualized by the amount of f-actin polarization they exhibit as compared to non-migrating cells.

While Tellam *et al.* does not specifically teach the proportions of fluorochrome labeled actin monomers which are added to the cellular lysate, the result-effective adjustment of conventional working parameters (e.g., determining an appropriate ratio of labeled actin monomer to endogenous actin) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

One of ordinary skill in the art at the time of the instant invention would have recognized that the compilation of reaction components into a centralized location for purposes of time efficiency and convenience would have been obvious and constitute a kit, in its broadest reasonable interpretation.

As Tellam *et al.* teaches a cell-re-suspension medium, substances necessary for the endogenous actin polymerization and protection of the lysate proteins, solutions of actin monomers labeled with a fluorochrome, the extracts of tumorigenic and non-tumorigenic cells and reaction buffers, the compilation of these components by one of skill in the art into a kit would have been an obvious time saving measure. There would have been a reasonable expectation of success in combining these two references because both are drawn to the detection and quantification of actin polymerization in cancerous cells.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 1-3 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malicka-Blaszkiewicz *et al.* (1995).

The teachings of Malicka-Blaszkiewicz *et al.* were discussed above.

Malicka-Blaszkiewicz *et al.* does not teach wherein the method is used to predict the sensitivity of the cells to a radiotherapy or chemotherapy anticancer treatment.

It would have been obvious to one of ordinary skill in the art at the time of the invention to adapt the method for the quantification of polymerized F-actin in cancerous and control cell lysate in the steady state to predict the sensitivity of the cells to a chemotherapy anticancer treatment because Malicka-Blaszkiewicz *et al.* discloses that the increased amount of actin polymerization is directly related to the increase in motility (invasiveness) and one of ordinary skill in the art would have been motivated to adapt the method to predicting the sensitivity of these cells to a chemotherapy anti-cancer treatment because of the benefit described by Malicka-Blaszkiewicz *et al.* of stopping or reversing the process of metastatic (cancerous) growth through the use of drugs (chemotherapy) affecting actin polymerization. There would have been a reasonable expectation of success in making this adaptation because the reference discloses possibility of generating new drugs using the actin polymerization measurement method.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

11/06/06

JON WEBER
SUPERVISORY PATENT EXAMINER